Kleinfeld Kaplan Becker
1850 M Street NW, Suite 1000
Washington, DC 20036
202.223.5120 › kkblaw.com

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Division of Dockets Management
Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, MD 20852

Citizen Petition

The undersigned, on behalf of a client, submits this Citizen Petition pursuant to 21 C.F.R. § 10.30 and Part 314, and Section 505 of the Federal Food, Drug, and Cosmetic Act ("FDCA"), 21 U.S.C. § 355 to assure that psychedelic drug products are uniformly subject to the same rigorous medical and scientific approval framework applicable to other classes of drugs.

Psychedelic substances have a long history of use for healing and spiritual purposes. More recently, there has been growing interest in and active research on the therapeutic potential of psychedelic drugs, often for treatment of serious, chronic mental health conditions. Responding to this interest, in 2023 FDA published draft guidance providing recommendations on the design of clinical trials for psychedelic drugs.[1] In early 2024, FDA convened a public workshop with the Reagan-Udall Foundation to discuss methods to address the challenges to designing clinical trials of this class of drugs highlighted in the draft guidance.[2] Later that year, FDA rejected the first New Drug Application ("NDA") seeking approval of a psychedelic drug, midomafetamine ("MDMA"), for treatment of post-traumatic stress disorder ("PTSD"), citing a failure to establish both effectiveness and safety. Encouraged by the promise of this new class of drugs, interest in investigating potential therapeutic applications of psychedelic drugs nevertheless persists despite this initial failure, and several clinical development programs are ongoing.

Earlier this year, President Trump issued an executive order intended to facilitate timely approval and commercialization of psychedelic drugs, in part through issuance of Commissioner's National Priority Vouchers ("CNPV"), which can substantially reduce the standard FDA review period for drug applications.[3] The following week, FDA announced issuance of three CNPVs to

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[1] Press Release, FDA Issues First Draft Guidance on Clinical Trials with Psychedelic Drugs (June 23, 2023), available at: https://www.fda.gov/news-events/press-announcements/fda-issues-first-draft-guidance-clinical-trials-psychedelic-drugs; *Psychedelic Drugs: Considerations for Clinical Investigations,* Draft Guidance (June 2023), available at: https://www.regulations.gov/document/FDA-2023-D-1987-0002 ("Draft Psychedelic Drugs Guidance").

[2] Public Workshop: Advancing Psychedelic Clinical Study Design, Jan. 31-Feb. 1, 2024, available at: https://www.fda.gov/news-events/fda-meetings-conferences-and-workshops/public-workshop-advancing-psychedelic-clinical-study-design-01312024#event-information; *Advancing Psychedelic Clinical Study Design,* Meeting Summary (June 2024), available at: https://reaganudall.org/sites/default/files/2024-06/Advancing%20Psychedelic%20Clinical%20Study%20Design_Meeting%20Summary%20%281%29.pdf

[3] Executive Order 14401, Accelerating Medical Treatments for Serious Mental Illness (April 18, 2026), available at: https://www.whitehouse.gov/presidential-actions/2026/04/accelerating-medical-treatments-for-serious-mental-illness/.

companies studying psychedelic therapies.[4] Three months later, FDA finalized its guidance on the design of clinical trials for psychedelic drugs.[5] Subsequently, FDA held a Part 15 hearing on therapeutic use of psychedelic drug products in supervised and supportive settings, and opened a docket for comments.[6] Despite these regulatory efforts, and intense interest from patients and clinicians, FDA has yet to approve an NDA for a psychedelic drug. However, FDA will soon be called upon to take action on this new class of drugs. Three sponsors, two of which hold CNPVs, have reportedly submitted NDAs to FDA:

- Usona Institute – original NDA for Psilocybin for major depressive disorder, granted a CNPV
- Resilient Pharmaceuticals (formerly Lykos Therapeutics) – resubmission of NDA for MDMA for PTSD, following 2024 rejection
- Compass Pathways – original NDA for Psilocybin (COMP360) for treatment-resistant depression, granted a CNPV

Petitioner applauds the efforts to facilitate development of psychedelic drug therapies and looks forward to FDA action on these pending applications, but seeks to ensure enthusiasm about these new medications does not lead to approvals based on thin data packages or inconsistently applied standards. In accordance with FDA's mandate of protecting and promoting public health, this citizen petition requests that FDA apply uniform, established statutory approval standards to review and action on these pending NDAs, and future NDAs seeking approval of psychedelic drug products.

I. Action Requested

Petitioner requests that the Food and Drug Administration take the following actions:

1. Apply established standards for demonstration of safety and effectiveness set out in the Federal Food, Drug, and Cosmetic Act and FDA's implementing regulations to all NDAs seeking approval of psychedelic drug products; and
2. Apply those established standards for demonstration of safety and effectiveness in a consistent fashion across all NDAs for psychedelic drug products, subjecting similarly situated applications to the same evidentiary expectations, requests, and standards.

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[4] FDA Accelerates Action on Treatments for Serious Mental Illness Following Executive Order (April 24, 2026), available at: https://www.fda.gov/news-events/press-announcements/fda-accelerates-action-treatments-serious-mental-illness-following-executive-order.

[5] *Psychedelic Drugs: Considerations for Clinical Investigations; Guidance for Industry* (July 2026) ("Psychedelic Drugs Guidance"), available at: https://www.fda.gov/media/169694/download.

[6] Considerations for Potential Future Therapeutic Use of Psychedelic Drugs; Public Hearing; Request for Comments, 91 Fed. Reg. 43095 (July 14, 2026); Considerations for Potential Future Therapeutic Use of Psychedelic Drugs, Public Hearing (Sept. 14, 2026), available at: https://www.fda.gov/news-events/fda-meetings-conferences-and-workshops/considerations-potential-future-therapeutic-use-psychedelic-drugs-public-hearing-09142026

II. Statement of Grounds

A. Legal and Regulatory Background

Under the FDCA, a "new drug" may not be introduced into interstate commerce unless FDA has approved an NDA for it. 21 U.S.C. § 355(a); 21 U.S.C. § 321(p) (defining "new drug" as one not generally recognized among qualified experts as safe and effective for its labeled use). An NDA must include full reports of investigations showing whether the drug is safe and effective for use; a full list of its components and a statement of its composition; a description of the methods, facilities, and controls used to manufacture, process, and pack it; samples as required; proposed labeling; and required patent information. 21 U.S.C. § 355(b)(1); 21 C.F.R. § 314.50.

After review, FDA either approves the NDA, or refuses approval, if any statutory ground for refusal applies. 21 U.S.C. § 355(c)–(d); 21 C.F.R. §§ 314.105, 314.125. Statutory grounds for refusing to approve an NDA include inadequate testing or insufficient evidence of safety; manufacturing methods, facilities, or controls inadequate to preserve the drug's identity, strength, quality, and purity; a lack of substantial evidence of effectiveness; or labeling that is false or misleading in any particular. 21 U.S.C. § 355(d); 21 C.F.R. § 314.125.

"Substantial evidence" of effectiveness requires evidence from adequate and well-controlled investigations, including clinical investigations, conducted by qualified experts. 21 U.S.C. § 355(d). While NDAs are typically supported by more than one large Phase 3 study, the "substantial evidence" standard may be satisfied by a single adequate and well-controlled clinical investigation plus confirmatory evidence, if FDA determines the data are sufficient to establish effectiveness. *Id.* FDA regulations detail the characteristics of an adequate and well-controlled study. 21 C.F.R. § 314.126.

Should FDA determine that an NDA does not satisfy statutory approval standards, the Agency issues a Complete Response Letter ("CRL") describing the deficiencies in the application and recommending actions the sponsor may take to place the application in condition for approval. 21 C.F.R. §§ 314.105, 314.110. After receipt of a CRL, an applicant may resubmit its NDA addressing the deficiencies identified in the CRL, withdraw its application, or request an opportunity for a hearing on the question of whether there are grounds for refusing approval. 21 C.F.R. § 314.110.

The same statutory standards for approval apply to all drugs, but the Agency exercises its scientific judgment to determine the nature and quantity of data necessary to satisfy those standards. 21 C.F.R. § 314.105(c). As noted above, in the case of psychedelic drugs, FDA has published guidance describing considerations that should be addressed in drug development programs, in light of the unique characteristics of psychedelic drugs and the methodological challenges they present. This guidance does not weaken or otherwise change established standards for safety or effectiveness, nor does Executive Order 14401 or the CNPV program.

In reviewing NDAs and other applications, FDA must treat applicants in a uniform and even-handed manner; it may not impose disparate standards on similar applications, absent a legitimate reason for the differing treatment.[7]

FDA may require a risk evaluation and mitigation strategy ("REMS") when such a strategy is necessary to ensure that the benefits of the drug outweigh its risks. 21 U.S.C. § 355-1. A REMS may include a variety of elements to mitigate risk, ranging from a medication guide to restrictions on the conditions under which a drug may be prescribed or dispensed. 21 U.S.C. §§ 355-1(e), (f).

B. At Least One Pending Application Appears Deficient In Light of Established Approval Standards

Certain of the NDAs reported to be pending before the Agency may not satisfy established approval standards. While publicly available information about these applications is quite limited, sufficient information concerning one NDA – that of Usona Institute, seeking approval for psilocybin for major depressive disorder – suggests deficiencies that FDA should carefully evaluate, with the goal of assuring that all NDAs are subject to established statutory approval standards, and within the particular class of psychedelic drugs, similarly situated applications are treated similarly.

Media reports indicate that Usona Institute ("Usona") has recently completed submission of an NDA for chemically synthesized psilocybin for treatment of major depressive disorder ("MDD"), a chronic condition.[8] It appears that the application rests on a single pivitol Phase 3 trial called uAspire and a Phase 2 study, PSIL201. Information on the uAspire study is limited to the clinicaltrials.gov entry[9] while the Phase 2 study is described in a clinicaltrials.gov entry which includes the protocol and statistical analysis plan[10] and a study publication.[11] These materials suggest significant gaps in the Usona clinical data package.

The uAspire study entailed randomization of 238 participants into one of three groups: psilocybin 25 mg, psilocybin 5 mg, or placebo. After an initial 43-day (roughly 6-week) double-

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[7] *See Bracco Diagnostics, Inc. v. Shalala*, 963 F. Supp. 20, 27-8 (D.D.C. 1997) (FDA's unexplained failure to treat similarly situated products in the same way was arbitrary and capricious in violation of the Administrative Procedure Act, stating, "What the FDA is not free to do, however, is to treat them dissimilarly and to permit two sets of similar products to run down two separate tracks, one more treacherous than the other, for no apparent reason"); s*ee also United States v. Diapulse Corp.,* 748 F.2d 56 (2d Cir. 1984) (holding that FDA must "apply its scientific conclusions evenhandedly" and cannot "'grant to one person the right to do that which it denies to another similarly situated'." (citation omitted)); *Allergan, Inc. v. Shalala,* No. 94-1223, 6 Food and Drug Rep. 389 (D.D.C. Nov. 10, 1994) (holding that FDA enforcement must be conducted in a fair and even handed manner against similarly situated parties; otherwise agency conduct is arbitrary and capricious in violation of the APA).

[8] *Usona Files Psilocybin for Depression NDA as Race With Compass Tightens*, Psychedelic Alpha, Nov. 2, 2026, available at: https://psychedelicalpha.com/news/usona-files-psilocybin-for-depression-nda-as-race-with-compass-tightens/.

[9] Available at: https://clinicaltrials.gov/study/NCT06308653.

[10] Available at: https://clinicaltrials.gov/study/NCT03866174.

[11] Raison CL, Sanacora G, Woolley J, et al. *Single-Dose Psilocybin Treatment for Major Depressive Disorder: A Randomized Clinical Trial*. JAMA. 2023;330(9):843–853, available at: https://jamanetwork.com/journals/jama/fullarticle/2808950.

blind period where participants received a single dose of their assigned treatment, all participants were to proceed into a 1-year follow-up period, during which eligible participants who meet pre-determined criteria may be offered open-label psilocybin 25 mg.

Treatments were to be administered in the context of a protocol for extensive psychosocial support consisting of (1) preparation with two facilitators prior to dosing, (2) administration of treatment in a 7-10 hour dosing session under the supervision of the two facilitators, and (3) 4 hours of post-dose integration sessions with the same two facilitators. The primary outcome measure is change in central rater Montgomery-Asberg Depression Rating Scale total score from baseline to Trial Day 43. The two secondary outcome measures are change in central rater Clinical Global Impression-Severity total score from baseline to Trial Day 43 and change in on-site rater administered Sheehan Disability Scale score from baseline to post-dose Day 43.

The clinicaltrials.gov entry for the uAspire trial was last updated on October 19, 2026 and currently specifies an estimated completion date of January 30, 2027.

The apparent gaps in the clinical data package are discussed below. Collectively, they suggest a data package that fails to satisfy the statutory standards for approval.

- Open-Label Follow-Up Period; Seemingly Incomplete Data

When a psychedelic drug is investigated for treatment of a condition that persists for months or years, such as MDD, the Psychedelic Drugs Guidance (p. 10) recommends sponsors evaluate the durability of response through a trial design that incorporates blinded, long-term follow-up, typically 12 months. Consistent with the Psychedelic Drugs Guidance, one of the primary bases for rejecting Lykos' original application for MDMA for treatment of PTSD was failure to demonstrate a durable treatment effect. FDA recommended a new clinical trial in which participants are followed in a blinded manner after the acute treatment period, with follow-up assessments scheduled at least monthly.[12] FDA's expectation for a long-term, blinded study period to demonstrate durability of response is consistent with its historical approach to clinical evaluation of therapies for chronic diseases.[13] Like the Lykos MDMA study, the uAspire study similarly does not demonstrate a durable treatment effect because the study entailed only a 6-week double-blind period, followed by an open-label 1-year follow-up period.

Even if the uAspire study design had included an appropriate, blinded 12-month follow-up period capable of demonstrating a durable treatment effect, it appears that any data currently before FDA would be insufficient. The clinicaltrials.gov record for the uAspire study indicates the study will not be complete for another two months, and Usona presumably required several months to analyze the data and prepare its NDA in advance of NDA submission reported on

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[12] Complete Response Letter, NDA 215455 (Aug. 8, 2024) ("Lykos CRL"), available at: https://download.open.fda.gov/crl/CRL_NDA215455_20240808.pdf.

[13] *See, e.g., Ulcerative Colitis: Developing Drugs for Treatment,* Draft Guidance, p. 4 (April 2022), available at: https://www.fda.gov/media/158016/download; *Neovascular Age-Related Macular Degeneration: Developing Drugs for Treatment,* Draft Guidance, pp. 3-4 (February 2023), available at: https://www.fda.gov/media/165606/download; *Crohn's Disease: Developing Drugs for Treatment,* Draft Guidance, p. 4 (April 2022); *Alcoholism: Developing Drugs for Treatment*, Draft Guidance, p. 5 (Feb. 2015), available at: https://www.fda.gov/media/91222/download.

November 2nd, suggesting the data from the single Phase 3 study was analyzed well before all patients completed their 1-year follow-up period.

- Abbreviated Double-Blind Evaluation Period

Both the Psychedelic Drugs Guidance (p. 10) and the 2023 Draft Psychedelic Drugs Guidance (p. 10) provide that studies evaluating psychedelic drugs for treatment of chronic illnesses, such as MDD, should entail a double-blind design in which treatment effect is evaluated at 12 weeks.[14] Notably, Usona was aware of this recommendation in the Draft Psychedelic Drugs Guidance, and submitted comments urging FDA to revise the draft to recommend studies in which the primary efficacy endpoint is assessed at 6 to 12 weeks, depending on the indication.[15] Despite this, Usona initiated its uAspire study over eight months after publication of the Draft Psychedelic Drugs Guidance,[16] using a design in which the primary and secondary endpoints were assessed at the conclusion of day 43 (roughly 6 weeks), following which an open-label follow-up period began. It is difficult to discern how effectiveness for a chronic condition could be adequately demonstrated through assessments after such a short, 6-week period, particularly when the follow up period was open-label.

- Failure to Isolate the Contribution of Psychotherapy

FDA regulations identifying the characteristics of an adequate and well-controlled study emphasize that the "purpose of conducting clinical investigations of a drug is to distinguish the effect of a drug from other influences, such as spontaneous change in the course of the disease, placebo effect, or biased observation." 21 C.F.R. § 314.126(a). The Psychedelic Drugs Guidance (p. 11), and the earlier Draft Psychedelic Drugs Guidance (p. 9) both acknowledge that many drug development programs include psychological support or psychotherapy during the dosing period or in a separate session, and both also note that this variable complicates assessment of effectiveness. Both guidance documents further provide that a factorial design may be useful to isolate the separate contributions of the investigational drug and psychotherapy to any observed treatment response. The Agency raised the same point in the Lykos CRL, recommending a new clinical trial characterizing the extent to which psychotherapy contributes to the treatment benefit, potentially with a factorial design that includes an arm with no psychotherapy. This approach is consistent with, and conceptually the same as, the Agency's long-standing requirement that investigations of a drug product containing two or more active ingredients should demonstrate the contribution of each active ingredient to the observed response from the combination, often through a factorial design.[17]

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[14] The recommended 12-week double-blind period is consistent with FDA's approach to other chronic conditions with subjective endpoints and a notable placebo response, *e.g.,* chronic pain. *Development of Non-Opioid Analgesics for Chronic Pain,* p. 10, Draft Guidance (May 2026), available at: https://www.fda.gov/media/188612/download.

[15] Comments of Usona Institute, Docket FDA-2023-D-1987 (Aug. 25, 2023), available at: https://www.regulations.gov/comment/FDA-2023-D-1987-0200.

[16] The clinicaltrials.gov entry for the uAspire study reflects an actual start date of March 13, 2024. *See* https://clinicaltrials.gov/study/NCT06308653.

[17] *See, e.g., Codevelopment of Two or More New Investigational Drugs for Use in Combination,* Guidance, pp. 7-9 (June 2013), available at: https://www.fda.gov/media/80100/download; *Hypertension: Developing Fixed-Combination Drug Products for Treatment,* Guidance, pp. 2-3 (Nov. 2018), available at: https://www.fda.gov/media/117975/download; *Development of Cancer Drugs for Use in Novel Combination -*

All three treatment arms of the uAspire study included the same protocol for psychosocial support before dosing, during the 7-10 hour dosing schedule, and during post-dosing integration sessions. As a result, the contribution of the extensive psychosocial support to the observed treatment effect is unknown.

- Inadequate Measures to Control Bias

FDA regulations provide that an adequate and well-controlled study must include adequate measures to minimize bias on the part of subjects, observers, and analysts of the data. 21 C.F.R. § 314.126(b)(5). Because psychedelic drugs are associated with intense perceptual changes, FDA recognizes that subjects, therapists, monitors, and/or raters may be able to determine whether a subject has received the investigational drug or placebo, functionally unblinding the study. The Agency recommends that steps be taken to minimize these potential biases, and cautions that data should be "strongly persuasive and robust across study endpoints to overcome biases that may be introduced by functional unblinding." *See* Psychedelic Drugs Guidance, p. 9.[18]

Focusing on psychosocial support, FDA concluded that therapists can generally deduce the treatment assigned through observation of the subject during dosing. For this reason, the Psychedelic Drugs Guidance (p. 11) and the predecessor Draft Psychedelic Drugs Guidance (p. 9) suggest that the in-session monitor not be involved in post-session therapy. This technique does not appear to have been employed in the uAspire study; instead, the clinicaltrials.gov record suggests that the same two facilitators participate in the sessions before, during, and after dosing, as was the case in the Usona Phase 2 study, PSIL201.[19]

The Psychedelic Drugs Guidance (p. 9) and the earlier Draft Psychedelic Drugs Guidance (p. 8), also recommend the use of a blinding questionnaire to determine whether subjects, observers and other participants believe the subject received the investigational drug or placebo, to aid in evaluating the impact of functional unblinding. Further, the Guidance (p. 10) notes that an expectancy evaluation questionnaire assessing subjects' expectations about potential drug effects before randomization and after treatment should be considered, to further aid in data interpretability despite functional unblinding. The clinicaltrials.gov record for uAspire makes no mention of either technique, nor do the materials describing the Phase 2 study, PSIL201. It is unknown whether or how Usona managed the bias introduced by functional unblinding.

Determining the Contribution of the Individual Drugs' Effects, Draft Guidance, p. 4 (July 2025), available at: https://www.fda.gov/media/187589/download.

[18] The earlier Draft Psychedelic Drugs Guidance (p. 8) also recognized the likelihood of functional unblinding due to the perceptual disturbances associated with psychedelic drugs. Similarly, the Agency's broadly applicable guidance on demonstration of effectiveness recognizes that a study may be unable to contribute to a finding of substantial evidence of effectiveness in circumstances where unblinding is common due to an effect of the drug, and the primary endpoint is subject to bias when treatment assignment is known. *Demonstrating Substantial Evidence of Effectiveness for Human Drug and Biological Products, Draft Guidance* (June 2026), pp. 6-7, available at: https://www.fda.gov/media/133660/download.

[19] Protocol, § 6.1, p. 62, available at: https://cdn.clinicaltrials.gov/large-docs/74/NCT03866174/Prot_000.pdf.

- Small Safety Database

An NDA must include information sufficient to enable FDA to conclude the drug is safe for its intended use. 21 U.S.C. § 355(d). The Agency has emphasized the need for a safety database of adequate size and duration to support a benefit-risk assessment and NDA approval.[20] With respect to psychedelic drugs in particular, FDA acknowledges that some theorize that one or a few doses may produce a durable therapeutic benefit, but nevertheless recommends sponsors evaluate the safety and efficacy of repeat dosing when investigating psychedelic drugs for treatment of chronic illnesses. *See* Psychedelic Drugs Guidance, p. 10.

The design of the uAspire study suggests an expectation that some subjects with MDD will benefit from a single dose of psilocybin, while others may require re-administration during the 12-month open-label follow-up period. FDA guidance applicable to drugs intended for long-term treatment, either chronic or repeated intermittent use for longer than 6 months, provides that the safety data base should include roughly 1500 exposed subjects, with 300-600 subjects exposed for 6 months and 100 subjects exposed for 12 months.[21] While these benchmarks may be unnecessarily high for a drug intended to be administered a few times, albeit for treatment of a chronic illness, the size of the Usona safety database appears to be unusually small, and may be inadequate to enable FDA to evaluate safety or to make an appropriate benefit-risk assessment.

- Potential Failure to Systematically Solicit and Record all Adverse Events

The Psychedelic Drugs Guidance (p. 8), as well as the Draft Psychedelic Drugs Guidance (p. 7), recommend that studies identify and document all central nervous system effects, including expected or "positive" psychoactive effects in order to ensure adverse events associated with abuse potential are monitored and recorded. Failure to collect information on events that subjects, therapists, or study physicians considered "positive" or "favorable," impeding FDA's ability to assess signals of abuse potential, was one of the primary bases for rejecting Lykos' application for MDMA for treatment of PTSD. Without this information, the Agency concluded that the Lykos studies did not adequately characterize the safety of MDMA. FDA recommended this deficiency be addressed through a new study in which all abuse-related adverse events are recorded, regardless of whether the events were considered untoward or desirable, with the nature, onset and resolution of each event characterized.[22]

No information on collection of adverse events in uAspire is available, but it appears that Usona's Phase 2 study did not systematically solicit positive/favorable central nervous system

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[20] *Demonstrating Substantial Evidence of Effectiveness for Human Drug and Biological Products*, Draft Guidance (June 2026), p. 16, available at: https://www.fda.gov/media/133660/download; *Demonstrating Substantial Evidence of Effectiveness With One Adequate and Well-Controlled Clinical Investigation and Confirmatory Evidence*, Draft Guidance (September 2023), p. 3, available at: https://www.fda.gov/media/172166/download.

[21] *E1A The Extent of Population Exposure to Assess Clinical Safety: For Drugs Intended for Long-term Treatment of Non-Life-Threatening Conditions*, Guidance (1995), available at: https://www.fda.gov/media/71180/download.

[22] Lykos CRL.

effects, but rather left the decision to the discretion of the investigator.[23] If uAspire did not entail systematic collection of all central nervous system effects, regardless of whether those effects were expected or viewed as favorable, the study does not adequately characterize the safety of psilocybin.

- Need for a REMS and Labeling Addressing Psychosocial Support/Psychotherapy

Both the Psychedelic Drugs Guidance (p. 13) and the predecessor draft (p. 11) indicate that a REMS may be needed for psychedelic drugs. Though Usona has not publicly commented on the REMS proposed in its NDA, media reports indicate Usona is in discussions with FDA concerning a REMS.[24] The uAspire and PSIL201 studies evaluated psilocybin in conjunction with extensive psychosocial support/psychotherapy and, as noted above, the contribution of that psychosocial support/psychotherapy to observed effectiveness and to safety has not been characterized. As a result, it is unknown whether psilocybin administered with a less comprehensive or different type of psychosocial support/psychotherapy would produce the same results.

For all of the reasons discussed above, the Usona NDA does not appear to be approvable, but were the Usona NDA to be resubmitted with further clinical data addressing these apparent gaps, the features of an appropriate REMS would still require careful consideration. A new clinical trial investigating psilocybin in the context of the same or similar type of extensive psychosocial support/psychotherapy studied in uAspire and PSIL201 would necessitate a REMS incorporating that psychosocial support/psychotherapy element. Relatedly, any approved labeling for the Usona product would also need to specify use of psilocybin in conjunction with the studied psychosocial support/psychotherapy component. 21 C.F.R. § 201.57(c)(2)(i)(A) ("[i]f the drug is used for an indication only in conjunction with a primary mode of therapy (e.g., diet, surgery, behavior changes, or some other drug), a statement that the drug is indicated as an adjunct to that mode of therapy" must appear in the indications section of the label).

III. Conclusion

Psychedelic drugs represent a promising new therapeutic class that may provide needed options for patients suffering from chronic, debilitating illnesses. That promise, however, should not be used to justify circumventing statutory approval standards applicable to other classes of drugs, or creating alternative, less regulated pathways for psychedelic access. Patients deserve, and the FDCA requires, that FDA approve only those applications supported by adequate safety and effectiveness data, consistent with the FDCA and FDA's implementing regulations. Only through adherence to those established standards can the Agency assure that patients are not exposed to risks that have not been adequately characterized, and do not forgo or delay treatments with proven benefit in favor of one whose effectiveness is uncertain.

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[23] Protocol, § 11.1.1, p. 92, available at: https://cdn.clinicaltrials.gov/large-docs/74/NCT03866174/Prot_000.pdf.

[24] *Usona Files Psilocybin for Depression NDA as Race With Compass Tightens*, Psychedelic Alpha, Nov. 2, 2026, available at: https://psychedelicalpha.com/news/usona-files-psilocybin-for-depression-nda-as-race-with-compass-tightens/.

The integrity of the FDCA approval standard is the bedrock on which public trust in medicine rests. To maintain this public confidence and promote public health, Petitioner requests that the Agency strictly apply established standards for demonstration of safety and effectiveness to the Usona NDA and all other NDAs seeking approval of psychedelic drug products, and take care to apply those established standards in a consistent fashion across all NDAs for psychedelic drug products, subjecting similarly situated applications to the same evidentiary expectations and requests.

IV. Environmental Impact

Petitioner claims a categorical exclusion from the requirements of an environmental assessment or environmental impact statement pursuant to 21 C.F.R. § 25.31.

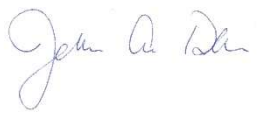
V. Economic Impact

An economic impact statement will be submitted if requested by the Commissioner, pursuant to 21 C.F.R. § 10.30(b).

VI. Certification

The undersigned certifies, that, to the best knowledge and belief of the undersigned, this petition includes all information and views on which the petition relies, and that it includes representative data and information known to the petitioner which are unfavorable to the petition.

Respectfully submitted,



Jennifer A. Davidson
Kleinfeld, Kaplan and Becker, LLP
1850 M Street, N.W., Suite 1000
Washington, DC 20036
Phone: 202-223-5120